document spotty hyperplasia of neural stem cells and a parallel loss of epithelium. This neural stem cell phenotype resembles the Notch-Delta neurogenic phenotype, so we have conducted genetic interactions with this pathway. Results imply that aqz interacts with this pathway.

doi:10.1016/j.ydbio.2011.05.221

Program/Abstract # 268
Neural crest and ectodermal contributions to the development of the nasal placode

Paolo Emanuele Forni[a], Carlor Taylor-Burds[b], Vida Senkus Melvin[c], Trevor Williams[c], Susan Wray[b]
[a]*NIH Cellular and Developmental Neurobiology Section NINDS, Bethesda, MD, USA*
[b]*CDNS/NINDS/NIH, Bethedsa, MD, USA*
[c]*Dept. of Craniofacial Biology and Dept. of Cell and Developmental Biology, Denver, CO, USA*

The lineage of nasal placode derivates such as olfactory ensheathing cells and GnRH-1 neurons has been debated for several decades. To analyzed neural crest and ectodermal contributions to the development of the nasal placode, cell fate tracing was performed using Wnt1Cre/Rosa and ectodermal Crect/Rosa mouse lines. Wnt1Cre recombination was found in cells commingled with the superficial ectoderm at E8.5 and in the developing placode starting from E9.5. Wnt1Cre recombination was found in the entire population of olfactory ensheathing cells and in subpopulations of GnRH-1 neurons, olfactory and vomeronasal cells. No ectopic Wnt1Cre expression was detected in the superficial ectoderm and in the developing placode. Analyzing the olfactory and GnRH-1 system in Crect/Rosa mutants established that the majority of sensory neurons and GnRH-1 cells were ectodermal derivatives and that subpopulations of both cell types were negative for ectodermal recombination. The Crect negative sensory cells and GnRH-1 cells were found in similar number to those positive for Wnt1Cre neural crest tracing. In addition, analysis after ectodermal tracing confirmed the exclusive neural crest origin of the olfactory ensheathing cells in mammals. These data indicate that the olfactory and GnRH-1 systems are composed of cells from both neural crest and ectodermal origin that mix in the developing nasal placode.

doi:10.1016/j.ydbio.2011.05.222

Program/Abstract # 269
A Bmp-Id2a-Twist1-Fli1a network specifies ectomesenchyme from cranial neural crest

Das Ankita
University of Southern California, Los Angeles, CA, USA

Vertebrate cranial neural crest cells (CNCCs) contribute not only to ectodermal lineages like neurons, glia and pigment but also to "ectomesenchymal" lineages like cartilage and bone. Whereas it has been previously proposed that signaling from the pharyngeal endoderm induces ectomesenchyme fates, we find that CNCCs express the ectomesenchyme-specific marker dlx2a in the absence of endoderm. Further, we show that downregulation of Bmp signaling in CNCCs as they migrate away from the neural tube is essential for ectomesenchyme formation. We find that in zebrafish, forced expression of Bmp4 in migratory CNCCs inhibits expression of the ectomesenchyme genes dlx2a and fli1a and prolongs expression of early CNCC genes sox10. Previous studies have shown a role for the bHLH transcription factor Twist1 in ectomesenchyme specification in mouse, and here we show in zebrafish that Bmp signaling functions to induce expression of id2a, an inhibitor of Twist1. id2a expression is restricted to the non-ectomesenchyme population, and forced expression of id2a or reduction of Twist1 in migratory CNCCs results in loss of fli1a expression and prolonged expression of sox10. Moreover, we find that increasing Bmp4, Id2a or decreasing Twist1 or Fli1a, results in similar losses of ectomesenchyme derived head skeleton and concomitant increases in glial fates. Furthermore, we have identified a Twist1-binding element in the enhancer of fli1a and suggest that fli1a is a likely direct target of Twist1. Hence, we propose a novel model of ectomesenchyme specification in which migration away from a Bmp signaling source at the neural-plate border is critical for CNCCs to downregulate id2a and activate the ectomesenchyme genes Twist1 and Fli1a.

doi:10.1016/j.ydbio.2011.05.223

Program/Abstract # 270
Understanding neural crest cell development using Gcnf−/− mutant mice as a model system

Annita Achilleos, Jennie Crane, Shachi Bhatt, Paul Trainor
Stowers Institute, Kansas City, MO, USA

The neural crest (NC) is a multipotent, migratory cell population that is a hallmark of vertebrate evolution and gives rise to a diverse array of tissues including peripheral nervous system and craniofacial skeleton. Formation of the NC encompasses several steps including induction and specification from a precursor pool, epithelial to mesenchymal transition (EMT) and emigration from the neural tube, migration and differentiation into diverse cell types. Previous work in aquatic and avian model systems has revealed that a gene regulatory network mediated by Wnt, BMP and FGF signaling drives NC formation. However, knockout mouse models have failed to recapitulate a role for these pathways in mammalian NC cell induction. We are currently using a mouse mutant in germ cell nuclear factor (Gcnf)/Nr6a1 to study mammalian NC formation. Analysis of Nr6a1−/− mutant embryos in our laboratory has revealed an absence of NC cells, which results from a failure of neural progenitors to differentiate into NC and undergo EMT. Along with our global gene expression and protein interaction analysis, our results revealed that Gcnf regulates two key processes during NC formation: stem cell maintenance and EMT. Therefore, we hypothesize that Gcnf acts as a bimodal switch (i) repressing pluripotency genes and activating NCC-specific genes during NCC formation and (ii) regulating EMT during NCC delamination. This is the first example of a complete absence of NC in a mammalian system. We will use Nr6a1−/− mice to identify the global gene and protein networks that regulate NC formation, which will further our understanding of the causes of neurocristopathies including craniofacial, cardiac and enteric congenital malformations.

doi:10.1016/j.ydbio.2011.05.224

Program/Abstract # 271
Characterization of downstream targets of Pax3 and Zic1 in the developing neural crest

Chang-Soo Hong[a], Jean-Pierre Saint-Jeannet[b]
[a]*Daegu University, Gyeongbuk, Republic of Korea*
[b]*University of Pennsylvania, Philadelphia, PA, USA*

In Xenopus, the neural plate border gives rise to at least three cell populations: the neural crest, the pre-placodal ectoderm and the hatching gland. The fate of these cells is largely dependent on the activity of two transcription factors, Pax3 and Zic1. Using gain of function and knockdown approaches in whole embryos we have previously shown that Pax3 and Zic1 are necessary and sufficient to promote hatching gland and pre-placodal fates, respectively, while the combined activity of Pax3 and Zic1 is essential to specify the